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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,828	06/27/2006	Carlos Garcia-Echeverria	33586-US-PCT	3954

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EXAMINER	
RAO, DEEPAK R	
ART UNIT	PAPER NUMBER
1624	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,828	GARCIA-ECHEVERRIA, CARLOS	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18-21 and 23-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,18-21 and 23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20060627*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15, 18-21 and 23-26 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-2, 15, 18-21 and 23-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound of formula (I) wherein the substituents $(R_1)_m$ (wherein m is 1-5) represent the independent substituent groups as defined in the claims, does not reasonably provide enablement for compounds of formula (I) wherein two vicinal R_1 substituents together with the carbon atoms of the phenyl ring (to which the two R_1 substituents are attached) form a heterocyclic ring. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the

above noted factual considerations.

The specification fails to enable the preparation of the entire scope of the claimed compounds. The process schemes in pages 14-23 of the specification, followed by the examples provide the essential starting materials to prepare the claimed compounds of formula (I). All the examples disclose compounds wherein R_1 represents the independent substituent groups, however, there is no disclosure of the sources of starting materials needed to prepare the compounds of formula (I) wherein two vicinal R_1 substituents together with the carbon atoms of the phenyl ring (to which the two R_1 substituents are attached) form a heterocyclic ring. The specification does not provide any explanation or sources of starting materials or the resulting products wherein two vicinal R_1 substituents together with the carbon atoms of the phenyl ring (to which the two R_1 substituents are attached) form a heterocyclic ring, such that a person of ordinary skill could determine which groups are suitable to prepare the instantly claimed compounds. For example, if one R_1 represents a group alkyl-sulfonyl and another represents amino-sulfonyl, then a cyclic group formed by the two R_1 groups together will have completely different structural features, which are not described in the schemes nor in the examples. The resulting compounds will have a different structural nucleus than that of formula (I). In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention. The starting material sources necessary to obtain the instant compounds must have been available as of the filing date in order to provide an enabling disclosure. See *In re Howarth*, 654 F.2d 103, 210 USPQ 689 (CCPA 1981); *Ex parte Moersch*,

104 USPQ 122 (POBA 1954). Applicants should show that the sources of these starting materials was common knowledge or readily available at the time of filing.

2. Claims 15, 18-21, 24 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising a compound of formula (I) and a carrier; or a method of treating breast cancer, does not reasonably provide enablement for a pharmaceutical composition which comprises a compound of formula (I) and an additional agent; or a method for treating a disease which responds to inhibition of IGF-1R; or a method for **preventing** or treating vein graft stenosis, restenosis and/or vascular occlusion. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claim 15 is drawn to "A compound .... for medical use". When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated

based on that limitation. See MPEP § 2164.01(c). In contrast, when a compound or composition claim is **not** limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for non-enablement based on how to use.

The instant claims 24 and 26 are drawn to 'a pharmaceutical composition comprising a compound of formula (I) together with inhibitors of the enzymes of polyamine synthesis, inhibitors of protein kinase C inhibitors of other tyrosine kinases, cytokines, … and/or cytostatic drugs' and the specification does not provide sufficient written description regarding such combination compositions. The specification on pages 28-33 provides various examples of the additional substance of the composition intended by the instant claims, however, the scope of the claims includes agents that are known and those that may be discovered in future, for which there is no enablement. Specifically, the examples in the specification include generic groups or agents such as antitumor antibiotics, cytostatic agents, etc. all of which include numerous species and there is insufficient guidance in the specification to enable one of ordinary skill in the art how the compounds of the invention and the other biological agent provide a synergistic activity to achieve the desired results.

The instant claim 20 is directed to 'a method of treating a disease or medical condition mediated alone or in part by IGF-1R tyrosine kinase'; and claim 19 is drawn to 'a method for **preventing** or treating vein graft stenosis, restenosis and/or vascular occlusion'. The specification at page 6 provides a wide variety of conditions for which the instant compounds may be used as therapeutic agents. The specification at pages 33-35 provides *in vitro* assays to measure the IGF-1R tyrosine kinase inhibition activity. Based on the inhibition activity, the

specification provides that the compounds are useful as inhibitors of IGF-1R tyrosine kinase, and therefore useful in the treatment of a variety of diseases, including all types of cancer. The instant claims appear to be 'reach through' claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or medical conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

The test data provided in the specification on pages 33-35 is related to inhibition of IGF-1R, and the instant claims on the other hand are drawn to 'method of treating tumors'; 'a method for **preventing** or treating vein graft stenosis, restenosis and/or vascular occlusion'; etc. Following the test procedures, the specification concludes that 'the compounds of the invention show therapeutic efficacy especially against proliferative diseases responsive to an inhibition of the IGF-1R tyrosine kinase', however, there is neither data on how many compounds were tested and which ones were not. Applicant did not state on record or provide any guidance that the assays provided are correlated to the clinical efficacy of the treatment of various disorders of the claims. As can be seen from specification, the *in vitro* activity data holds significant role in determining the dosage regimen based on the minimal effective concentration of each of the compound to achieve the desired modulation of IGF-1R.

The instant claims include: 'a method of treating a disease which responds to inhibition of IGF-1R' which includes 'a method of treating tumors'; 'a method for **preventing** or treating vein graft stenosis, restenosis and/or vascular occlusion'. First, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no

enablement provided. The use disclosed in the specification is as IGF-1R inhibitors, in the treatment of a large list of diseases, which include proliferative diseases such as tumors. There is nothing in the disclosure regarding how the disclosed *in vitro* data correlates to the treatment of the various disorders encompassed by the instant claims. The diseases encompassed by the instant claims include various types of cancer, some of which have been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

Further, the instant claims recite 'a method of treating a disease which responds to the inhibition of IGF-1R'; 'a method for **preventing** or treating vein graft stenosis, restenosis and/or vascular occlusion', and thereby encompasses a method treating of a large list of diseases due to that activity (some of which are disclosed in the specification at page 6), and there is no disclosure regarding how all these assorted types diseases are treated. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor activity is generally unpredictable and highly structure specific area. It is inconceivable as to how the claimed compounds can treat the large list of diseases embraced by the claims having diverse mechanisms. The state of the art is indicative of the unpredictability of the therapeutic approach based on kinase inhibiting activity. LeRoith et al. (Cancer Letters 2003) indicate that 'studies suggest a role for IGF-1 as a risk factor for breast, colorectal, and lung cancer, but its utility as a pragmatic marker is potentially limited by ethnic and gender

factors' (see page 134). Further, the reference provides that: "It has been suggested that the IGF-1R itself can function as an oncogene, based upon the phenotype of fibroblasts overexpressing the IGF-1R. However, the relevance of this system to human cancer in general is unclear" (see page 134). The article concludes with the remarks that: "A better understanding of this complex system will facilitate the development of novel approaches to diagnose and treat various human cancers" (see page 135). Thereby the state of the art is indicative of the burden of undue experimentation for one skilled in the art to practice the instantly claimed methods.

The instant claims include 'treating or **preventing** cancer'. A 'cancer' or 'tumor growth' is anything that causes abnormal tissue growth. That can be growth by cellular proliferation more rapidly than normal, or continued growth after the stimulus that initiated the new growth has ceased, or lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such term covers not only all cancers, but also covers precancerous conditions such as lumps, lesions, polyps, etc. No compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology. The state of the art is not indicative any pharmaceutical agents that are useful in the treatment of cancer generally. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to

establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally.

The diagnosis of each of the disease is generally suggested by medical history and reports of endoscopy, cytology, X-ray, biopsy, etc. depending on the symptoms, signs and complications, which is essential to establish the dosage regimen for appropriate treatment or prevention. The disclosure does not provide any guidance towards the dosage regimen required to facilitate the treatment and/or inhibition of the claimed disorders, nor indicate competent technical references in the appropriate methods.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Further, the instant claims are drawn not only to 'a method for treatment' but also to '**a method for prevention**', for which the specification does not provide sufficient enablement. 'To prevent' actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the recited effect of **prevention**. Based on the inhibitory activity, the instant compounds are disclosed to be useful in the "prevention" of, for example, degenerative disorders, for which applicants provide no competent evidence. It is inconceivable

from the *in vitro* data of a small number of representative compounds can be correlated to the "treating or **preventing**" of the various claimed disorders, such that the claimed compounds can not only treat but also "prevent" a myriad of diseases associated with the stated activity. Further, there is no evidence on record which demonstrates that the *in-vitro* screening test relied upon is recognized in the art as being reasonably predictive of success in any of the contemplated areas of "preventing". Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility, and not "warranting further study").

Part of the difficulty of developing drugs effective for **preventing** any of the medical conditions such as cancers, tumors, etc. lies in the lack of understanding as to why people come down with these disorders and the numerous causes of these disorders.

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

MPEP § 2164.01(a) states that "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)". That conclusion is clearly justified here and undue experimentation will be required to practice the claimed invention.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and

"predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 4, 7-15, 18, 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. Claim 2 is drawn to a compound of formula (Ib) wherein the substituent " Z " is at the 3-position (or *meta*-position) on the phenyl ring with respect to the point of attachment to the pyrazolyl ring. The claim recites that "the compound {4-[3-(4-Benzyloxy-phenyl)-1H-pyrazol-4-yl]-pyrimidin-2-yl}-[4-(2-dimethylamino-ethoxy)-phenyl]-amine is excluded". The excluded compound contains the Z substituent (i.e., benzyloxy group) at the 4-position (or *para* position). There is insufficient antecedent basis for this limitation in the claim because the claim specifically recites formula (Ib) which contains the benzyloxy group at a different position than the excluded compound.
2. In claim 4, line 2, the recitation "R1 is is" is redundant. The claim should be corrected by replacing the above with -- ~~R1~~ $\underline{R_1}$ is ~~is~~ --.

3. Regarding claim 18, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).
4. Claim 15 provides for the use of the compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

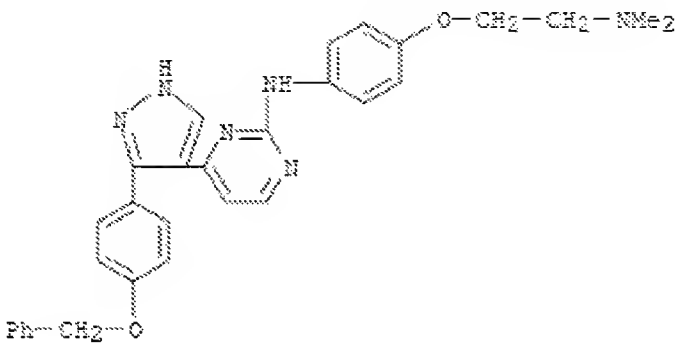
Claim 15 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 15, 18-20, 25 and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Furet et al., WO 2004/005282 (International filing date: July 8, 2003). The instant claims read on reference disclosed compound, see the compounds of formula (I) in page 1 and the corresponding species of Example 23 (structure depicted below for convenience):



The compounds are disclosed to be useful as pharmaceutical therapeutic agents for the treatment of, for example, breast cancer, see pages 6-7. Claims 20 and 18-19 recite 'treating a disease which responds to inhibition of IGF-1R' and the specification provides that the diseases include, for example, breast cancer. Therefore, claims 20 and 18-19 are drawn to a method wherein the compound is administered to the same patient population as disclosed for the reference compounds.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15, 18-21 and 23-26 are rejected under 35 U.S.C. 103(a) as being obvious over Furet et al., WO 2004/005282.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The reference teaches a generic group of pyrazolo-pyrimidine compounds, which embraces applicant's instantly claimed compounds. See formula (I) in page 1, and the species of

the Examples. The compounds are taught to be useful as pharmaceutical agents, see pages 6-7. The instant claims differ from the reference by reciting specific species or a more limited subgenus than the reference. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole i.e., as therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Alternatively, the reference taught pyrazolo-pyrimidine compounds and the instantly claimed compounds are structurally analogous. See the structural formula (I) in page 1 and the corresponding species, for example, the compound of Example 23. The compounds are taught to be useful as pharmaceutical therapeutic agents, see pages 6-7. The instant claims exclude the reference disclosed compound of Example 23, see the proviso in the claim. The instant claims, however, include compounds wherein Z is attached at a position different from the reference disclosed compound, i.e., at the 3-position as compared to the 4-position for reference compound and therefore, the instantly claimed compounds are positional isomers of the reference compounds. It would have been obvious to one having ordinary skill in the art at the time of the

invention to prepare the instantly claimed compounds because they are positional isomers of the reference compounds. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such isomeric compounds are suggestive of one another and would be expected to share similar properties and therefore, the same use as taught for the reference compounds, i.e., as pharmaceutical agents. It has been held that a compound, which is structurally isomeric with a compound of prior art is prima facie obvious absent unexpected results. *In re Finley*, 81 USPQ 383 (CCPA 1949); *In re Norris*, 84 USPQ 458 (CCPA 1950); *In re Dillon*, 919 F.2d at 696, 16 USPQ2d at 1904 (Fed. Cir. 1990).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15, 18-21, and 23-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over pending claims 1-11, 13 and 14 of copending Application No. 10/520,567. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims substantially overlap and/or structurally analogous to the compounds of the reference claims, see the claims in each of the application. The instantly claimed genus of formula (I) encompasses the compounds of the reference application. (See the reasons provided under 35 U.S.C. 103 rejection above). It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the compounds from the reference claims, including those instantly claimed, because the skilled artisan would have had the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole i.e., as pharmaceutical therapeutic agents. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Receipt is acknowledged of the Information Disclosure Statement filed on June 27, 2006 and a copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

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